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Periodontal disease effect on cardiovascular system

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Abstract
Periodontal disease (PD) is a complex chronic inflammatory disease involving bacterial activity and resulting in destruction of the tissues that support the teeth. This study was performed to analyse the effect of periodontal disease on cardiovascular diseases.The major connection between gum disease and heart disease is that bacteria from the mouth enter the bloodstream through the gums and oral bacteria stick to fatty plaques in the bloodstream, directly contributing to blockages. Oral bacteria also trigger an inflammatory response, causing the blood vessels to swell, reducing blood flow and increasing risk of clots. From the study the major conclusions made is treatments aimed at decreasing periodontal oinfection and inflammation can reduce serum inflammatory biomarkers predictive of cardiovascular disease and improve vascular responses. The cardiologists are advised to educate their patients on the role of maintaining oral health for general health and to refer to the periodontist when needed. At the same time the general dentists and the periodontists are advised to keep a check on the inflammation and maintain a zero tolerance for bleeding gums to prevent the risk of percolation of bacteria to other sites in the body.

Keywords: periodontal disease, cardiovascular disease, oral bacteria

Introduction
Oral disease particularly periodontal disease may place certain patients at increased risk of developing cardiovascular disease and stroke. An association exists between periodontal disease and cardiovascular disease. It is unknown whether this relationship is causal or coincidental. Most studies demonstrated positive associations between periodontal disease and cardiovascular disease. More recent studies have enhanced the specificity of infectious exposure definitions by measuring systemic antibodies to selected periodontal pathogens or by directly measuring and quantifying oral Microbiota from sub gingival dental plaque.
Results from these studies have shown positive associations between periodontal disease and cardiovascular disease. Inflammation referring to a protective tissue response to injury has been implicated in the pathogenesis of many human diseases. It plays a central role in complex multifactorial chronic inflammatory diseases including periodontitis and cardiovascular disease (CVD).
The word 'periodontium' means structures surrounding the teeth (i.e.) 'peri'- 'around' and 'odontos'- teeth. It comprises of four tissues – gingiva (the investing tissue), periodontal ligament, cementum and alveolar bone [15]
Periodontal disease is a common chronic inflammatory condition characterised by destruction of the tooth supporting structures due to bacterial infection [18].
Cardiovascular disease is a class of disease that affects the heart and/or blood vessels. These forms include high blood pressure, coronary heart disease (acute heart attack and angina pectoris), stroke, and heart failure. Studies have shown that there is a link between cardiovascular disease and periodontal (gum) disease, the chronic inflammation and infection of the gums and surrounding tissue. Forms of gum disease, such as gingivitis (gum inflammation) and periodontitis (bone loss), can be indicators for cardiovascular problems. It has been suggested that the inflammatory proteins and bacteria associated with gum disease enter a person's bloodstream and can cause various effects on the cardiovascular system [19].
Cardiovascular disease (CVD) and periodontitis are both chronic inflammatory disorders which are highly prevalent in populations. Bacteria involved in the periodontal disease have been found to be cardiovascular risk markers.
The inflammatory proteins and bacteria associated with gum disease enter a person's bloodstream and can cause various effects on the cardiovascular system. The bacteria known to cause periodontitis was associated with an increased level of blood vessel thickening [19]. Periodontal pathogens may contribute to the atheroma pathogenesis. Severe periodontitis is correlated with the prevalence of bacteraemia, and poor periodontal status is an important risk factor for CVD [14].
Epidemiological associations between periodontitis and cardiovascular disease have been reported. This could be directly due to periodontal pathogens or their products on endothelial cells via transient bacteraemia or indirectly due to products of the inflammatory response, central role in pathogenesis of cardiovascular disease. Periodontitis and atherosclerosis have complex aetiologies, genetic and gender predispositions and may share pathogenic mechanisms as well as common risk factors.
Several short term invention studies have reported that treatment of periodontitis reduces the serum concentrations of inflammatory markers. Studies have linked several of risk factors to periodontal disease, including diabetes, smoking, age, gender, and low score economic status [6] which is why it is important for individuals at risk for cardiovascular disease to visit a dentist on a regular basis, practice good oral hygiene, and keep their dentist informed of any oral and overall health issues [19].

Disease

Periodontal disease (PD) is a complex chronic inflammatory disease involving bacterial activity and resulting in destruction of the tissues that support the teeth [2].

Periodontal disease is a contagious, chronic bacterial infection that affects the gum tissue, bone and attachment fibres that support the teeth and hold them in place. Gum disease starts slowly without any pain and may not be apparent until there are serious side effects. Over time, a build-up of plaque bacteria (white, sticky substance) collects at the gum line, eventually hardening on the teeth into calcium deposits called calculus or tartar. Brushing and flossing cannot remove hardened plaque. If the tartar isn't removed with professional scaling by a dental hygienist, the bacteria can cause inflammation of the gums (gingivitis), penetrate the gum line and finally spread into the underlying bone (periodontitis). If left untreated, gum disease can result in abscesses or the complete destruction of the tooth's supporting tissues and, ultimately, tooth loss. Bacteria from diseased gums can contribute to the formation of artery clogging plaques (fatty deposits) perhaps leading to a heart attack or stroke. Also, some oral bacteria may cause infective endocarditis, a condition in which the interior lining of the heart and heart valves becomes inflamed. Left untreated, this condition could cause permanent heart damage or death [12].

Causes

- Inflammation is the body's natural response to an infection. Experts think that as inflamed blood vessels swell less blood may flow to the heart and the rest of the body, raising blood pressure. Bacteria may enter the bloodstream through the gums and become part of fatty plaques (a buildup of fat, cholesterol, calcium and other substances) in blood vessels. A stroke occurs when fatty plaques break off the wall of a blood vessel and travel to the brain cutting off its blood supply. A heart attack occurs when fatty plaques block a blood vessel leading to the heart.
- Smoking is related to gum disease, heart disease and stroke. Smoking weakens your body's immune system. This makes it harder to fight off a gum infection. Once you have gum damage, smoking also makes it harder for your gums to heal. Nicotine in tobacco causes blood vessels to constrict. As vessels narrow, blood pressure rises. Undetected or uncontrolled high blood pressure leads to heart disease, stroke, kidney failure and premature death. Quitting smoking and maintaining a healthy blood pressure through diet, exercise and nutrition may reduce the risk of developing heart disease and stroke (18).
- Local colonisation of dental plaque-forming bacteria, systemic conditions including diabetes mellitus, osteoporosis, rheumatoid arthritis and respiratory diseases are associated with the aetiology of PD, whereas age, ethnicity, sex, smoking, stress and poor coping behaviour, and obesity have a key role in the development of the disease [22].

Transmission

Periodontitis has a well-established bacterial aetiology.15 Periodontopathic bacteria include amongst others: P gingivalis (Pg), Tannerella forsythia (Tf) and Aggregatibacter actinomycetemcomitans (Aa). 4 infection in a susceptible host by theseputative pathogens elicits the release of an arsenal of weaponery such as leukotoxins, collagenases and proteases. Their presence precipitates an immune response that may be the means by which the atherogenic process is stimulated. These well-established periodontal pathogens have also been isolated from atheromatous plaques of the coronary circulation, aortic and heart valves (10). According to the most recent National Health and Nutrition Examination Survey (NHANES III) carried out between 1988 and 1994, 34.5% of dentate U.S. citizens 30years or older had periodontitis. The prevalence of periodontitis increased with increasing age (Albandar *et al*, 1999) and in developed countries, cardiovascular disease accounts for 50% of deaths (WHO report, 1995) and is considered the number one cause of death in the U.S. (Rosenberg *et al*, 1996).These data are consistent with the notion that both diseases are relatively prevalent and, as such, these findings could confound studies that seek to demonstrate a true relationship between cardiovascular disease and periodontitis (statistical alone or actually causal). Nevertheless, there are now several studies that seem to indicate that there are associations between cardiovascular disease and periodontitis [25].

Pathophysiology

The inflammation begins in the gingiva initially and remains confined to it. Most of the time the condition is reversible. When allowed to progress, periodontal inflammation sets in with gradual destruction of the supporting tissues over time and the condition is characterized by irreversible loss of the supporting tissues of the teeth. Though periodontitis is initiated by microbes, the progression and destruction of the tissues is predominantly due to the reactive host response to microbial attack ('by stander damage'). Page and Kornman showed a new dimension depicting the central role of inflammation in the pathogenesis of periodontal disease [7]. When bacterial biofilms (initiating factor for gingivitis and periodontitis) on the teeth are not physically disrupted on a regular basis, it leads to the emergence of gram negative bacteria. As a result of chronic bacterial challenge, inflammation is triggered leading to a series of events and the condition perpetuating from a stage of gingivitis (confined to gingiva) to periodontitis. Bacteria and their toxins (especially endotoxin) stimulate a localized tissue response causing the release of various cytokines and other mediators of inflammation. Chronic damage of epithelial tissues and the underlying connective tissues due toperiodontitis may induce the periodontal pocket (pathological deepening of the gingival sulcus) to ulcerate, allowing their access to the bloodstream. All these processes can disrupt the homeostasis when toxins gain entry into the systemic circulation. The proinflammatory cytokines TNF-á (tumour necrosis factoralpha), IL-1a (interleukin-1 beta), gamma interferon and PGE2 (prostaglandin E2) reach a high tissue concentration in periodontitis. The periodontium thus serves as a renewing reservoir for these mediators,that is spilled over into systemic circulation thereby inducing and perpetuating the systemic effects. IL-1afavors coagulation, thrombosis and retards fibrinolysis. Chemical mediators IL-1, TNF-á, and thromboxane can cause platelet aggregation and adhesion, formation of lipid-laden foam cells and deposition of cholesterol in the arteries. One may debate that an individual may have other infections but why the specific association of periodontitis with coronary artery disease [1]. The reason being the enormous bacterial load in

diseased periodontium, a source for infection for continuous release into systemic circulation. The total surface area of the diseased pocket epithelium in contact with sub-gingival bacteria and their products in a patient with generalized moderate periodontitis has been estimated to be approximately the size of the palm of an adult hand with even larger areas of exposure in cases of more advanced periodontal destruction [8]. They present a continually renewing reservoir of lipopolysacchride (LPS) and other gram-negative bacteria with ready access to the periodontal tissues and the circulation. When the surface area of dento-gingival epithelium exposed to bacterial invasion or infiltration of microbial antigenic components in periodontitis patients was calculated, the surface area of the inflamed portion was found to be ranging between 8 and 20 centimeter square. Systemic challenge with predominantly gram-negative bacteria induce major vascular response that includes inflammatory cell infiltrate into the vessel walls, vascular smooth muscle proliferation, vascular fatty degeneration and intravascular coagulation. In addition, LPS up regulates the expression of endothelial cell adhesion molecules [17].

Pathophysiological pathways

Various pathogenic mechanisms have been proposed to explain the association between PD and CVD. These mechanisms may individually or jointly contribute to a plausible association.

1. Effects of periodontal bacteria on platelets: Porphyromonas gingivalis and Streptococcus sanguis have been shown to stimulate platelet aggregation and thrombosis [16].
2. Autoimmune reactions / molecular mimicry: Crossreacting antibodies to periodontal bacteria and human heat shock proteins (HSPs) including HSP60 on endothelial cells have been recognised. These autoimmune responses could provoke endothelial damage and atherosclerosis. Invasion and/or uptake of periodontal bacteria in endothelial cells and phagocytes: Specific periodontal pathogens and their components have been identified in human atheromatous tissues. For instance, P. gingivalis and A. actinomycetemcomitans were present in atheromatous plaque of 79% and 67% patients.
3. Systemic inflammation: Both PD and CVD have been associated with increased systemic inflammatory markers such as C-reactive protein (CRP), which has also been indicated as an independent predictor of future CVD20 [22].

Several microorganisms have been described as causing PD, particularly Porphyromonas gingivalis. Bacteria produce endotoxins in the form of lipopolysaccharides (LPS) capable of triggering release of several different proinflammatory cytokines that are involved in the immunopathology of periodontitis and also in systemic responses to oral inflammatory processes.Examples include interleukin 1 beta (IL 1β), IL-6, tumor necrosis factor alpha (TNF-α), CRP and neutrophils.Chronic inflammation associated with bacterial plaque is predominantly caused by gram-negative bacteria. After the inflammatory stimulus there is increased production of prostaglandin E2 (PGE2) and of matrix metalloproteinases (MMP), which lead to extracellular destruction of the gingiva and the periodontal ligament, stimulating resorption of alveolar bone. Concurrent growth of anaerobic bacteria can promote formation of periodontal pockets. The inflammatory process at the periodontium leads to an increase in concentrations of CRP, and of other mediators such as fibrinogen, causing a systemic response [24]. Periodontal disease is also capable of affecting the emergence and severity of certain systemic diseases, including CVDs.In addition to increased cytokine concentrations, MMP levels also rise. All of the MMPs are important in the immunoresponse, but MMP-8 is the only proteinase that is able to fragment types I and III collagen, which are important for maintaining the structure of teeth. Thus, the higher the concentration of MMP-8, the worse the prognosis of PD. There are also correlations between periodontitis severity and concentrations of MMP-13, MMP-3, MMP-2 and MMP-1.3 The effect of bacterial proliferation and release of MMPs is activation of multiple cells, such as fibroblasts, keratinocytes, macrophages and endothelial cells. Bone resorption takes place as a result of fragmentation of the elements of the extracellular matrix by osteoclasts.The inflammatory process is dependent on a multiplicity of internal and external factors. Controllable risk factors include smoking, stress, poor oral hygiene and infrequent visits to the Dentist. Non-controllable risk factors include heredity, systemic diseases and age. The genetic component does not cause the disease; however it does make patients more susceptible to emergence of periodontal pathologies or to more serious disease course. Certain pathogens, such as Porphyromonas gingivalis, Tanerella forsythia and Fusobacterium nucleatum, can also influence disease severity. Stress also contributes to increasing the incidence of PD by creating conditions of resistance to glucocorticoids and increased IL-1, IL-6 and TNF-α production,caused by a dysfunction of CD11b monocytes in response to microbial products.Stress leads to down regulation of genes that are activated by glucocorticoids and act to suppress the immunoresponse, while up-regulating genes that cause exacerbation of the inflammatory process, both of which are factors that explain the intimate relationship between stress and PD.Stressed patients tend to adopt habits that worsen the health of their teeth, such as defective oral hygiene, smoking more than average and negative changes to dietary habits. The relationship between PD and AD can be explained by the action of circulating inflammatory cytokines that stimulate atherogenesis, or by the direct action of pathogenic bacteria that penetrate the circulatory system via the inflamed gingival tissues. One hypothetical model with a biological basis is the suggestion that individuals with cardiac and periodontal diseases have an exacerbated immunoresponse to bacterial infections.This response is caused by an abnormality of monocytic cell secretory capacity, by which these cells release high levels of proinflammatory mediators, such as PGE-2, IL-1β and TNF-α. People who have the hyperinflammatory monocyte phenotype secrete from three to ten times more mediators in response to bacterial lipopolysaccharides, when compared with people who are phenotypically normal.According to Seymour and Steele,there is evidence that patients with aggressive forms of periodontitis have this hyperinflammatory phenotype. Thus, the interaction between bacterial lipopolysaccharides and the monocytes that release a range of different cytokines is fundamental to initiation and progression of PD and also to its systemic effects, such as atherogenesis and thrombogenesis. Elevated

CRP concentrations increase the risk of cardiovascular events by 1.9 times. In addition to CRP, which has been discussed above, there are other proteins that also react to inflammation in the periodontium. Results for plasma fibrinogen tests, white blood cell counts and von Willebrand factor assays are all elevated in patients with periodontal problems. Additionally, people who have PD and elevated concentrations of acute phase proteins, such as CRP, fibrinogen, serum amyloid type 1, an adhesion molecules ICAM-1, E-Selectin and VCAM-1, are more likely to develop atherosclerosis and cardiovascular diseases.Fibrinogen is produced by hepatocytes in response to the action of cytokines, especially IL-6. Plasma fibrinogen concentrations are increased during chronic inflammations and infections, creating a hypercoagulable state. Thrombogenesis is related to atherogenesis and to growth of atherosclerotic plaques. Fibrinogen and fibrin, in turn, interact with monocytes, increasing production of IL-1β, which is an important mediator.According to a study conducted by de Oliveira,the worse a person's oral hygiene, the higher the concentrations of CRP and fibrinogen, and the greater the risk of cardiovascular events. There were differences between groups with good dental hygiene (CRP: 3.07 mg/L) and individuals who brushed their teeth less than once per day (CRP: 4.18 mg/L; $P<0.05$); and the same was true of fibrinogen, which was at higher concentrations in the group with poor oral hygiene (2.86 g/L × 2.98 g/L; $P<0.05$). While treating PD results in a transitory increase in proinflammatory cytokine levels, which is probably related to manipulation of the inflamed tissues and transitory bacteremia, inflammatory activity normalizes in 24 to 48 hours and, over the long term, if PD responds to treatment then concentrations of these cytokines will reduce.55 The NHANES I study56 detected a 25% increase in the relative risk of CAD among patients with periodontitis. Relative risks for angina and for fatal coronary events were 1.5 and 1.9, respectively.57 Periodontal disease is associated with a 19% increase in the risk of cardiovascular disease and this risk is even higher in the population aged less than 65 years, among whom relative risk is increased by as much as 44%.58 Periodontal pathogens colonizing atherosclerotic plaques can be observed throughout the circulatory system. Invasion of the artery wall by Porphyromonas gingivalis, for example, provokes endothelial expression of adhesion molecules such as IL-6, IL-1β and TNF-α. There is then recruitment of monocytes, and increase in expression of endothelial adhesion molecules and increased uptake of lipids by macrophages.41 The bacterial agents most frequently identified in atherosclerotic plaques are Porphyromonas gingivalis (32%); Aggregatibacter actinomycetencomitans (4%); Prevotella intermédia (20%), and Treponema denticola (32%). Administration of systemic antibiotics to patients with periodontitis resulted in reductions in the levels of systemic markers of inflammation.A review of the results from around 90 thousand patients with periodontitis found that relative risk of CVD was 120% higher in the affected group, when compared with controls.According to Hung *et al*,periodontitis increases the relative risk of PAD by 1.4 to 2.6 times. According to Balan,PD can be considered a weak independent risk factor for CVD, with relative risk around 24 to 35% higher than normal. However, according to some authors the relationship between periodontitis and CVDs is still unproven.Confounding factors prevent clear conclusions from being drawn because both AD and PD Share common risk factors. One example of this is smoking, which increases the incidence both of PD and of AD and could give a false impression that atherosclerosis increases the incidence of periodontitis or vice-versa.62 Implementation of a strategy to combat the processes of disease in teeth and their repercussions on other body systems will demand a change in habits and customs, which may imply increased investment in preservation of natural teeth. Health professionals will therefore have to illustrate to the population the importance of preserving natural teeth even if this demands greater care and expenditure on each individual person's health. In order to achieve this, health services must implement strategies designed to facilitate access to dental care, in particular for less privileged populations, among which the prevalence of periodontal diseases is higher. It is sometimes difficult to deal with this paradigm and it is even possible to find authors publishing in the medical Periodental disease and Atheros clerosis literature who argue against preservation of natural teeth on the basis that someone who has no teeth also has no PD and is therefore at lower risk of the systemic repercussions of periodontitis. Working from the same principal, perhaps they will also begin to recommend removing kidneys to avoid kidney stones or removing the heart to avoid myocardial infarction [2].

Clinical presentation

- Red, swollen or tender gums
- Gums that bleed when brushing or flossing
- Receding gums Deep pockets (the space between the gums and the teeth)
- Metallic taste
- Tooth sensitivity for no apparent reason
- Loose or shifting teeth
- Abscesses
- Pus around gums and teeth
- Chronic bad breath [12]
- Chest discomfort - Most heart attacks involve discomfort in the center of the chest that lasts more than a few minutes, or that goes away and comes back.
- It can feel like uncomfortable pressure, squeezing, fullness or pain.
- Discomfort in other areas of the upper body - Symptoms can include pain or discomfort in one or both arms, the back, neck, jaw or stomach.
- Shortness of breath with or without chest discomfort.
- Other signs may include breaking out in a cold sweat, nausea or light headedness [18].

Treatment

Non-Pharmacological treatment

- Effective prevention and early treatment of periodontitis may have an important role in reducing an individual's susceptibility to ACVD events and also in contributing to improved cardiovascular health at a population level. Patients should therefore be advised about the health risk associated with untreated periodontitis, particularly if they have other ACVD risk factors, and offered comprehensive periodontal care and advice. In patients who have suffered an ACVD event, good oral hygiene should be established and periodontal treatment staggered over several sessions, in order to minimize the magnitude of any intra-

operative bacteraemia and the subsequent inflammatory sequelae [4].

- The need for definitive restoration or extraction of the infected tooth, the primary source of odontogenic infection is readily apparent. Deep periodontal scaling and endodontic treatment with root filling are required in most instances.The key for the prevention and control of dental caries and advanced periodontitis is the active promotion of oral hygiene that include:rigorous brushing and dental flossing after each meal dietary counseling to reduce the indigestion of carbohydrates-rich foods or beverages use of topical fluorides and oral antimicrobial rinses such as chlorhexidine for patients at high risk for dental cariesbehavioral modification of risk factors, such as tobacco smoking overcoming the reluctance for regular visits to dental professions.Vaccine based on various immunogens derived from S.mutans,the principal bacterial agent associated with dental caries have been explored [11].
- Eliminate smoking and improve your overall health. Smoking is related to gum disease, heart disease and stroke. Smoking weakens your body's immune system. This makes it harder to fight off a gum infection. Once you have gum damage, smoking also makes it harder for your gums to heal. Nicotine in tobacco causes blood vessels to constrict. As vessels narrow, blood pressure rises. Undetected or uncontrolled high blood pressure leads to heart disease, stroke, kidney failure and premature death. Quitting smoking and maintaining a healthy blood pressure through diet, exercise and nutrition may reduce the risk of developing heart disease and stroke [18].
- Practicing proper oral hygiene is essential to maintaining healthy gums. This includes flossing regularly, brushing twice a day with antibacterial toothpaste, and visiting a dentist at least every six months. A healthy diet and regular exercise can help improve both your cardiovascular health and your overall health.
- It is important to keep all medical professionals up-to-date on your oral and overall health issues. Inform your physician if you have been diagnosed with a form of periodontal disease or are experiencing any issues with gum inflammation. Likewise, inform your dentist if you have been diagnosed with any form of cardiovascular disease, have experienced any cardiovascular problems, or have a family history of cardiovascular disease [21].
- Reduce their total calorie intake and consumption of foods high in cholesterol, saturated- and trans-fatty acids, and salt.
- Increase their consumption of foods with low saturated fat and high fibre.
- Control their weight via increased daily physical activity and reduced total calorie intake [22].

Pharmacological treatment

For both caries prevention and the treatment of the periodontitis, the most important strategy is the effective control of the supraginival and subgingival plaques through active promotion of and meticulous attention to oral hygiene. The diet should be scrutinized to eliminate or discourage frequent snaking or carbohydrate-rich foods or intake of sugar containing beverages. Various antiseptic and antimicrobial regimens are employed for the prevention of dental caries and treatment of different clinical forms of periodontal disease. Fluoride-containing dentifrices (e.g.1.1 sodium fluoride or 0.4% stannous fluoride) and dental flossing should be encouraged after each meal. Oral antimicrobial rinses with 0.12% chlorhexidine are also effective for the control of dental plaque bacteria that lead to caries.

Chlorhexidine acts as cationic detergent that kills a wide range of bacteria and is retained on the oral surfaces for prolonged periods to prevent plaque advancement. A synergistic antibacterial effect has been demonstrated with the combination of chlorhexidine and fluoride, greater than either agent alone.Prolonged application may also promote the emergence of resistant microorganisms. Among topical antibiotics, although both penicillin and tetracycline have cariostatic effects in animal models, only the topical, only the topical application of vancomycin has been shown to reduce dental caries with some degree of success in humans. Antibiotics of choice include penicillin plus metronidazole, or with clindamycin, or with ampicillin sulbactam. Acute necrotizing ulcerative gingivitis responds well to metronidazole alone. Clindamycin, ampicillinsulbactam, oramoxicillin-calvulanate is an alternative choice Certain types of severe periodontitis are amenable to systemic antimicrobial therapy in conjunction with mechanical debridement (scalling and root planning).This protocol has often obviate the need for radical surgical resection of periodontal tissues. In double- blind clinical studies of advanced periodontitis, systemic metronidazole (500 mg PO three times daily) or doxycycline (200 mg PO twice daily) for 1 to 2 weeks in conjunction with rigorous mechanical debridement of the root surfaces was found to reduce the need for radical surgery by 8%% in comparison of debridement plus placebo [11].

Results and Discussion

At a minimum, periodontal infections are epidemiologically associated with cardiovascular diseases, that is, periodontal diseases seem to be found more frequently in patients with cardiovascular diseases.

The connection between periodontal disease and cardiovascular system is that bacteria found in infected gum tissue around teeth break down the barrier between the gums and the underlying connective tissue, causing inflammation. During normal chewing or brushing, bacteria can enter the bloodstream and move to other parts of the circulatory system, contributing to the formation of cardiovascular disease. or swelling, is the body's natural response to infection. It is possible that as oral bacteria travel through the body it triggers a similar response, which then leads to the formation of arterial plaque. Oral bacteria have been found in the fatty deposits of people with atherosclerosis. These deposits can narrow arteries or break loose and clog them entirely, leading to heart attack or stroke.

The connection between gum disease and heart disease is that:

- Bacteria from the mouth enter the bloodstream through the gums.
- Oral bacteria stick to fatty plaques in the bloodstream, directly contributing to blockages.
- Oral bacteria trigger an inflammatory response, causing the blood vessels to swell, reducing blood flow and increasing risk of clots [24].

Ischemic heart disease, consisting of a decrease in myocardial perfusion, is mainly due to arteriosclerosis. Factors that favour its occurrence are age, male sex, hypercholesterolemia, tobacco, diabetes, obesity and chronic infections. Many of these are common risk factors in periodontal disease. Periodontal inflammation can cause a systemic inflammatory response, as evidenced by increases in C- reactive protein. Pathogens related to periodontal disease such as P. gingivalis, Tannerellaforsythia and A. actiomycetemcomitans have been found in atherosclerotic plaques and there is evidence that P. gingivalis can adhere and infect endothelial cells with consequent activation and expression of molecular adhesion cells. These findings make the relationship between periodontal disease and atherosclerosis more evident, since endothelial dysfunction seems to be an early fact in the development of atherosclerosis and it also predicts the instability of the plaque and they show the causal relationship between periodontal disease and atherosclerosis. Moreover, there are other studies reporting that individuals with high levels of LDL cholesterol and ischemic heart disease present deeper periodontal pockets than control patients.

Beck, *et al*. (2001) described that in patients with periodontitis and insulin-dependent diabetes may exist an abnormal cytokine secretion, which may present a high risk of ischemic heart disease.

Herzberg and Meyer (1996) inoculated rabbits with S. sanguis and it was observed a rapid platelet aggregation with alterations in the ECG, blood pressure and the cardiac contractility. Only certain pathogenic strains of the bacteria can lead to cardiovascular diseases. For example various strains of Pg induce varying responses in endothelial dysfunction which is the hallmark of CHD [13]. Periodontitis and CHD are both of immune-inflammatory origin and there are confounding risk factors like smoking, age and other systemic diseases like diabetes. These factors need to be taken into account while evaluating the further studies to prevent independent occurrence of periodontitis and CHD due to such confounding risk factors [17].

Conclusion

Inflammation plays a central role in atherogenesis from endothelial cell expression of adhesion molecules to the development of the fatty streak, established plaque, and finally plaque rupture. Human observational studies and experimental animal models continue to implicate periodontal infection as a systemic exposure that may perpetuate these inflammatory events in vessels. Although treatments aimed at decreasing periodontal infection and inflammation can reduce serum inflammatory biomarkers predictive of cardiovascular disease and improve vascular responses, the clinical relevance of these surrogate changes to reduced risks for myocardial infarction or stroke are not known at this time. Nevertheless, clinicians and patients should be knowledgeable about this consistent association and the potential preventive benefits of periodontal interventions [12]. Periodontal inflammatory response could exacerbate vascular inflammation via secreted cytokines that ultimately modulate atherosclerosis and CVD. The inflammatory cytokine IL-6 and TNFα, and CRP levels in serum increased are association with CVD and periodontal diseases. Periodontal intervention had a positive impact on the established risk factors for CVD to reduce inflammatory responses. Periodontal intervention studies have strengthened the evidence for an association between the periodontal disease and CVD, and have also indicated a causal link. As some periodontal procedures may increase bacteremia temporarily, effective antibiotic prophylaxis is necessary to the prevention bacteremia and the onset of CVD. However, detailed mechanism of spontaneous periodontal disease induces bacteremia and the influence of periodontal intervention procedures inducing bacteremia leading to CVD is unknown. Because of these different research results, carefully designed randomized trials based on this concept with longer follow-up and clinical observation are required to prove if periodontal intervention combined with drug therapy would reduce the incidence of CVD [14]. Although intervention studies and epidemiological data suggest that these is a strong correlation between periodontitis and CHD; *in vitro*, animal and long term clinical studies do not support the interaction and the exact biological mechanism of the pathogenesis of the spread of the disease. However in the interest of the patient's health, the cardiologists are advised to educate their patients on the role of maintaining oral health for general health and to refer to the periodontist when needed. At the same time the general dentists and the periodontists are advised to keep a check on the inflammation and maintain a zero tolerance for bleeding gums to prevent the percolation of septicemia from oral tissues to distant sites [17].

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Conflict of interest

There is no conflict of interest in our study.

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